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However, the presently claimed invention is: An isolated pathogenic *Leptospira* bacterium that is serologically cross-reactive to the *Leptospira* strain WKID (AGAL Accession No. N95/69684). In order to be an anticipatory reference, the single reference cited by the Examiner must disclose each and every element of the claims. *Hybritech v. Monoclonal Antibodies*, 231 USPQ 81 (Fed. Cir. 1986). There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 18 USPQ2d 1896 (Fed. Cir. 1991).

The *Leptospira* strain WKID represents a new grouping of *Leptospira fainei* which was identified by the Applicant on the basis of partial sequencing (bases 51-199) and pathogen-specific PCR of the first four isolates of this grouping.

Hookey (EMBL Z21634) identified a type of *Leptospira inadai*, several serovars of which are now recognized. These serovars are unrelated serologically to serovar hurstbridge and, contrary to what the Examiner says, Applicant has provided data showing a lack of cross-reactivity between the *Leptospira* strain WKID and *Leptospira inadai* isolates. As explained at page 43 of the Specification and at point 15 of the enclosed Declaration, Applicant sent one of the first isolates of serovar hurstbridge to the Leptospirosis Reference Library in Brisbane, Australia, in February 1994 to determine its serological cross-reactivity to other Leptospires. The report dated March 3, 1994 stated that the "culture was sero-negative to our main panel of serovars". The isolate was later tested against antisera to all 23 available serogroups of Leptospires at the Pasteur Institute in Paris. In both cases, antiserum to serovar Lyme was part of the panel tested, as were antisera to the six other serogroups listed above. However, no serological cross-reactivity between serovar hurstbridge and serovar Lyme was ever detected. This, then, is incontrovertible evidence that Hookey (EMBL Z21634) does not anticipate the presently claimed invention, because *L. inadai* is not: An isolated pathogenic *Leptospira* bacterium that is serologically cross-reactive to the *Leptospira* strain WKID (AGAL Accession No. N95/69684). Applicants would like the Examiner to note that in contrast to the **genetic** classification of Leptospires based on 16S rRNA gene sequence as taught by Hookey et al. or Perolat et al (EMBL U60594), the **serological** classification of Leptospires is based upon agglutinating epitopes of the surface lipopolysaccharide (LPS) of the various isolates. Thus,

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while serovar Lyme and serovar hurstbridge possess some identity in their rRNA gene sequences, such information is not predictive of an antigenic relationship.

Rejection under 35 U.S.C. §102(b)

The Examiner has maintained his rejection of Claims 1-6, 10 and 19 under 35 U.S.C. §102(b) as being anticipated by Perolat et al. (Abstracts). The Examiner maintains that the Perolat Abstract teaches the molecular and phenotypic characterization of Hurstbridge strains as a new genomic species of pathogenic *Leptospira*.

However, as stated above, In order to be an anticipatory reference, the single reference cited by the Examiner must disclose each and every element of the claims. *Hybritech v. Monoclonal Antibodies*, 231 USPQ 81 (Fed. Cir. 1986). There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 18 USPQ2d 1896 (Fed. Cir. 1991).

Perolat et al (Abstracts) teaches only that a grouping of Leptospires exists which is a new genomic species of the pathogenic *Leptospira* and that this grouping does not cross react with antisera to serovars representative of 23 recognized pathogenic serogroups. They do not teach: An isolated pathogenic *Leptospira* bacterium that is serologically cross-reactive to the *Leptospira* strain WKID (AGAL Accession No. N95/69684). In fact, they do not teach a specific microbe (by depositing it), how to isolate it, or any type of sequence. The microbe which is taught in Perolat et al (Abstract) is a grouping of *Leptospira* which grows at 13 and 30°C; azaguanine test, does not cross-agglutinate with 23 pathogenic serogroups and the main saprophytic ones, and does not share certain molecular characteristics with previous grouping of Leptospires. There is no molecular data presented which could be used to re-isolate and identify this microbe. The abstract merely states that molecular data such as RFLP and PCR fingerprints show the clonality of the new grouping and that the group does not share molecular characteristics with other known Leptospires. However, the new RFLP pattern of the group and/or the new PCR fingerprint is not presented. Thus, this could be any number of *Leptospire* groupings which are now known and does not anticipate: An isolated pathogenic *Leptospira* bacterium that is serologically cross-reactive to the *Leptospira* strain WKID (AGAL Accession No. N95/69684).

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Rejection under 35 U.S.C. §103(a)

The Examiner has maintained his rejection of Claims 7 and 9 as being unpatentable under 35 U.S.C. §103(a) over Hookey (EMBL Z21634) or Perolat et al. (Abstracts) in view of Chappel et al. (Manipulating Pig Production).

Further, the Examiner has maintained his rejection of Claims 8 and 11-14 as being unpatentable under 35 U.S.C. §103(a) over Hookey (EMBL Z21634) or Perolat et al. (Abstracts) in view of Chappel et al. (Manipulating Pig Production).

However, as noted in the rejections under 35 U.S.C. §102 above, Hookey et al teaches *Leptosira* serovar Lyme which is not cross-reactive to *Leptospira* strain WKID (AGAL Accession No. N95/69684).

Further, Perolat et al (Abstracts) teaches only that a grouping of Leptospires exists which is a new genomic species of the pathogenic *Leptospira* and that this grouping does not cross react with antisera to serovars representative of 23 recognized pathogenic serogroups. They do not teach: An isolated pathogenic *Leptospira* bacterium that is serologically cross-reactive to the *Leptospira* strain WKID (AGAL Accession No. N95/69684).

Chappel et al. (Manipulating Pig Production) merely teaches that *Leptospira* bacterium may cause human infection, making it an important field of research. In addition, the Examiner believes that Chappel et al. teaches that reproductive problems are well known to be associated with *Leptospira* infections in pigs and bovines.

In order to establish a *prima facie* case of obviousness (MPEP ¶2143):

First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure (*In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1440 (Fed. Cir. 1991)).

Failure to establish any one of these three requirements precludes a finding of a *prima facie* case and, without more, entitles Applicant to allowance of the claims at issue.

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As stated above, the combination of Hookey (EMBL Z21634) or Perolat et al. (Abstracts) with Chappel et al. (Manipulating Pig Production) does not teach all of the claimed elements because it does not teach: An isolated pathogenic *Leptospira* bacterium that is serologically cross-reactive to the *Leptospira* strain WKID (AGAL Accession No. N95/69684). In fact, Hookey teaches a different strain which was shown by the Applicants to posses no cross-reactivity, and Perolat teaches only that a new strain or grouping which does not cross-react with the known strains of Leptospires exists, but does not identify them in any way which one of skill in the art would be able to use to distinguish them. Chappel et al teaches only that Leptospires cause disease in humans.

For the same reason, Applicants maintain that the combination of Hookey (EMBL Z21634) or Perolat et al. (Abstracts) in view of Chappel et al. (Manipulating Pig Production) do not render Claims 8 and 11-14 unpatentable under 35 U.S.C. §103(a) because Chappel et al. only teaches that reproductive problems are well known to be associated with *Leptospira* infections in pigs and bovines, and thus, the combination does not teach An isolated pathogenic *Leptospira* bacterium that is serologically cross-reactive to the *Leptospira* strain WKID (AGAL Accession No. N95/69684), which is capable of infecting bovines.

Rejection under 35 U.S.C. §103(a)

The Examiner has maintained his rejection of Claims 5-8, 10, 12, 75 and 124-126 as being unpatentable under 35 U.S.C. §103(a) over Hookey (EMBL Z21634) or Perolat et al. (Abstracts) in view of Haake et al. (US Patent 6,643,754). The Examiner believes that, in addition to the teaching by Hookey and Perolat, Haake teaches that Leptospire compositions may induce an immune response in animals.

As noted in the rejection under 35 U.S.C. §102 and in the enclosed Declaration, Hookey et al teaches *Leptosira* serovar Lyme which is not cross-reactive with *Leptospira* strain WKID (AGAL Accession No. N95/69684).

Further, as noted in the rejection under 35 U.S.C. §102, Perolat et al (Abstracts) teaches only that a new grouping of Leptospires exists which is a new genomic species of the pathogenic *Leptospira* and that this grouping does not cross react with antisera to serovars representative of 23 recognized pathogenic serogroups. Perolat (Abstracts) does not teach a method for identifying this grouping and, and thus, they do not teach: An isolated pathogenic *Leptospira*

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bacterium that is serologically cross-reactive to the *Leptospira* strain WKID (AGAL Accession No. N95/69684).

Haake teaches that preparations of outer membrane portion of Leptospires may induce an immune response in animals

Therefore, the combination of Hookey (EMBL Z21634) or Perolat et al. (Abstracts) with Haake does not teach all of the claimed elements because it does not teach An isolated pathogenic *Leptospira* bacterium that is serologically cross-reactive to the *Leptospira* strain WKID (AGAL Accession No. N95/69684). In fact, Hookey teaches a different strain which was shown by the Applicants to posses no cross-reactivity, Perolat teaches only that a new strain or grouping which does not cross-react with the known strains of Leptospires exists, and Haake et al teaches only that Leptospire preparations may induce an immune response in animals.

Conclusion

For the reasons set forth above, it is respectfully submitted that Applicants' claims as amended should be passed to allowance. Should there be any questions regarding the above-identified patent application, the Examiner is respectfully requested to contact the undersigned at the telephone number below. Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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